

We will start momentarily at 2pm ET



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Elizabeth Thompson,
unemployed chemist



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Travel Award to Summer 2014 London Science Forum

April 25, 2014; 3:00pm EDT



ACS International Center™
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Richard O'Kennedy, Ph.D.
Biochemist
President, London International Youth Science Forum

www.acs.org/ic_london

The **London International Youth Science Forum (LIYSF)** is a two-week scientific conference with attendees from all over the world. Learn about this summer's upcoming forum, **July 23-August 6, 2014**, and how you can apply for a travel award to take you there.



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We appreciate your patience while we work to complete the migration of past and current episodes, which we hope to have available as soon as possible.

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Upcoming ACS Webinars®

www.acs.org/acswebinars.



Thursday, April 3, 2014

“Detecting Human Exposure to Environmental Toxins”

Elizabeth Hamelin, Centers for Disease Control and Prevention
Lucas Zarwell, Chief Toxicologist, District of Columbia



Thursday, April 10, 2014

“The Chemistry of Cocktails: Bruising and Louching and Fire Oh My!”

Darcy J. Gentleman, Ph.D, Science communicator, ACS Office of Public Affairs
Kathryn Verona, ACS Office of Public Affairs

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Next in the 2014 Drug Discovery Series!



Session 3: Thursday, April 24, 2014

“Key Concepts in Identifying Drug Leads”

Chris Lipinski, Melior Discovery

Dr. Tudor Oprea, UNM School of Medicine, DTU Center for Biological Sequence Analysis

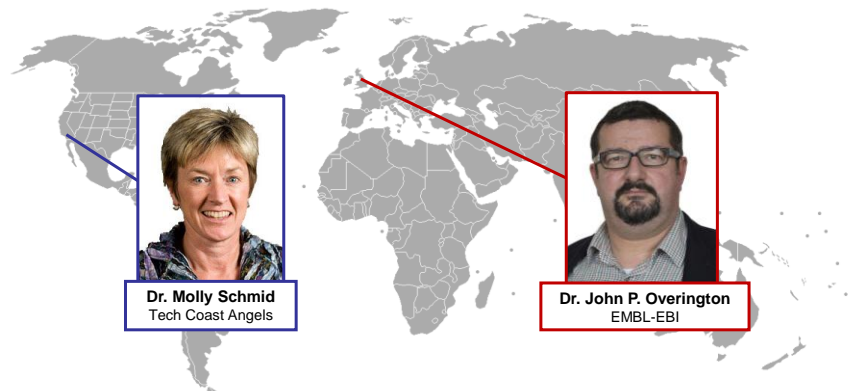
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**2014 Drug Discovery Series:
Session 2: Primer in Drug Target Classes**



Dr. Molly Schmid
Tech Coast Angels



Dr. John P. Overington
EMBL-EBI

Slides Available Now! All recordings will be available to only ACS Members.

<http://acswebinars.org/drug-discovery>

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Primer in Drug Target Classes

ACS webinars - 2014 Drug Discovery Series
Session 2: March 27th 2014

John P. Overington
EMBL-EBI

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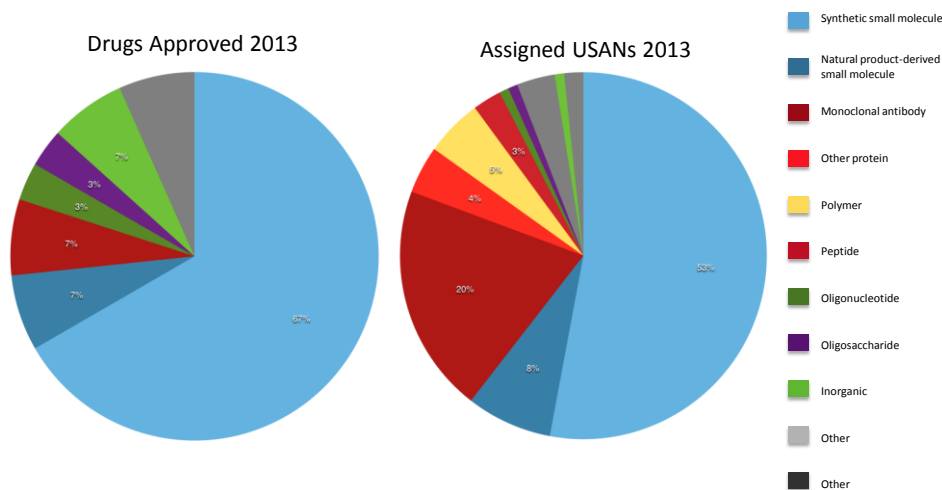
linkedin: uk.linkedin.com/in/joverington/

welcometrust

EMBL



Different Types of Drugs



Santos et al, unpublished

The screenshot displays the ChEMBL website interface. At the top, there is a search bar and navigation links. Below, a chemical structure is shown in a 3D viewer. To the right, there is a 'List Search' section. Below the viewer, a table of drug data is visible, with columns for 'Molecule Name', 'ATC Code', 'Molecular Weight', 'Target Name', 'Active Type', 'Organism', 'Binding Site', and 'Molecular Weight'. The table lists several molecules, including 'Small molecule 2013', 'Allylglycine', and 'Dimethyl Fumarate'.

ChEMBL

<https://www.ebi.ac.uk/chembl>

- The world's largest primary public database of medicinal chemistry data
 - ~1.4 million compounds, ~9,000 targets, ~12 million bioactivities
- Truly Open Data - CC-BY-SA license
- ChEMBL data also loaded into BindingDB, PubChem BioAssay and BARD

A. Gaulton et al (2012) *Nucleic Acids Research Database Issue*. 40 D1100-1107

Assay Organism Data

The screenshot displays the ChEMBL Target Search interface. On the left, a taxonomic tree shows the hierarchy of organisms, with 'Eukaryotes (713)' selected. A blue arrow points from this category to the search results table. The table lists target results for 'CHEMBL Target Search Results: 4649'. The columns include ChEMBL ID, Preferred Name, UniProt Accession, Target Type, Organism, Compounds, and Bioassays. The results are filtered to show 'Homo sapiens' as the organism.

ChEMBL ID	Preferred Name	UniProt Accession	Target Type	Organism	Compounds	Bioassays
CHEMBL38	Acetylcholinesterase HSA	Q0389	SINGLE PROTEIN	Plasmodium vivax	10	12
CHEMBL37	Transporter	Q12479	SINGLE PROTEIN	Musca domestica	97	97
CHEMBL36	UDP-glucosyltransferase 2B4	P01030	SINGLE PROTEIN	Homo sapiens	91	117
CHEMBL35	Glucosyl-uridylyltransferase-uridylylase L3	E13243	SINGLE PROTEIN	Homo sapiens	19	23
CHEMBL34	SRH1955-esterase domain class 19A4	Q91046	SINGLE PROTEIN	Homo sapiens	88	88
CHEMBL33	Winged domain serine-proteinase 2	E13205	SINGLE PROTEIN	Homo sapiens	1	1
CHEMBL32	UDP-glucosyltransferase 2B8	Q01731	SINGLE PROTEIN	Homo sapiens	9	9
CHEMBL31	Serine/threonine-protein kinase Spk3	Q98211	SINGLE PROTEIN	Homo sapiens	940	1101
CHEMBL30	NAD-dependent methyl-lysine methyltransferase	Q13738	SINGLE PROTEIN	Homo sapiens	6	10
CHEMBL29	NAD kinase	Q0564	SINGLE PROTEIN	Homo sapiens	16	20

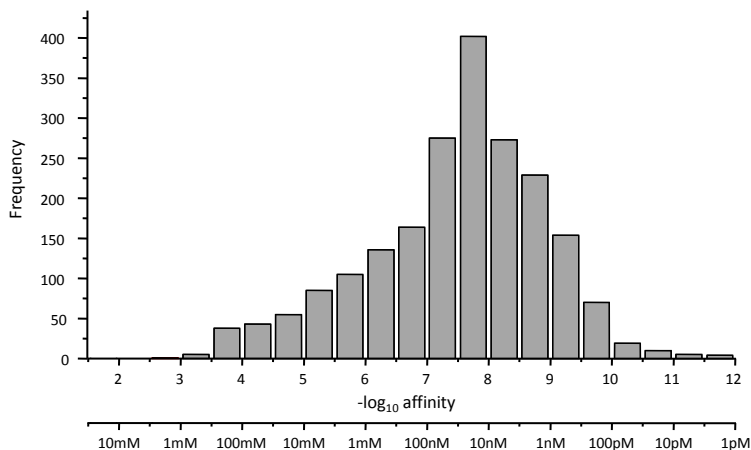
Drug Approvals

The screenshot displays the ChEMBL Drug Approvals page. The table lists FDA drug approvals for New Molecular Entities (NMEs) from 2009 onwards. The columns include Generic Name, Trade Name, ATC Code, Date of Approval, and Drug Monograph. The table is filtered to show 'Homo sapiens' as the organism.

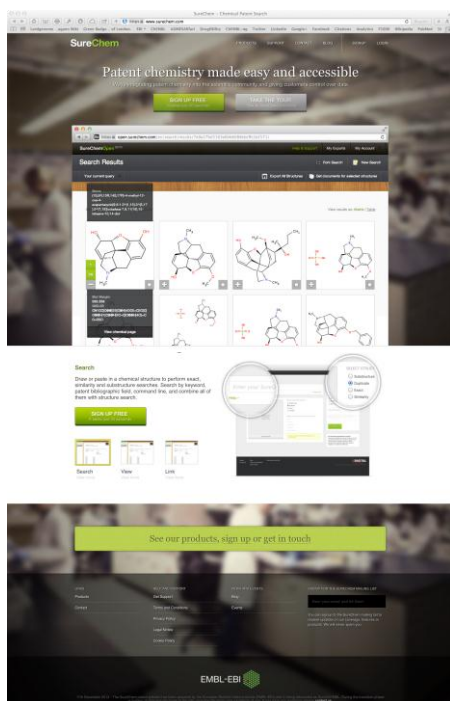
Generic Name	Trade Name	ATC Code	Date of Approval	Drug Monograph	Icon
Aminin Divaloate	Gilertif	L01XE13	2013-07-12	http://chembl.blogspot.co.uk/2013/07/new-drug-approvals-2013-07-12.html	
Dabrafenib Mesylate	Tafinlar	L01XE23	2013-05-29	http://chembl.blogspot.co.uk/2013/05/new-drug-approvals-2013-05-29.html	
Trametinib Dimethyl Sulfoxide	Mekinist	L01XE26	2013-05-29	http://chembl.blogspot.co.uk/2013/05/new-drug-approvals-2013-05-29.html	
Radium Ra 223 Dichloride	Xeljfo	V10X03	2013-05-15	http://chembl.blogspot.co.uk/2013/05/new-drug-approvals-2013-05-15.html	
Vandetanib Trifluoroacetate	Breo Elipha	R03AK10	2013-05-10	http://chembl.blogspot.co.uk/2013/05/new-drug-approvals-2013-05-10.html	
Caragliflozin	Invokana	A10BX11	2013-03-29	http://chembl.blogspot.co.uk/2013/04/new-drug-approvals-2013-03-29.html	
Oxalate Ester Meglumine	Dotarem	V03CA02	2013-03-20	http://chembl.blogspot.co.uk/2013/03/new-drug-approvals-2013-03-20.html	

Affinity of Drugs for their ‘Targets’

K_i , K_d , IC_{50} , EC_{50} , & pA_2 endpoints for drugs against their ‘efficacy targets’



Overington, *et al*, *Nature Rev. Drug Disc.* **5** pp. 993-996 (2006) Gleeson *et al*, *Nature Rev. Drug Disc.* **10** pp. 197-208 (2011)



SureChEMBL

<https://www.surechembl.org>

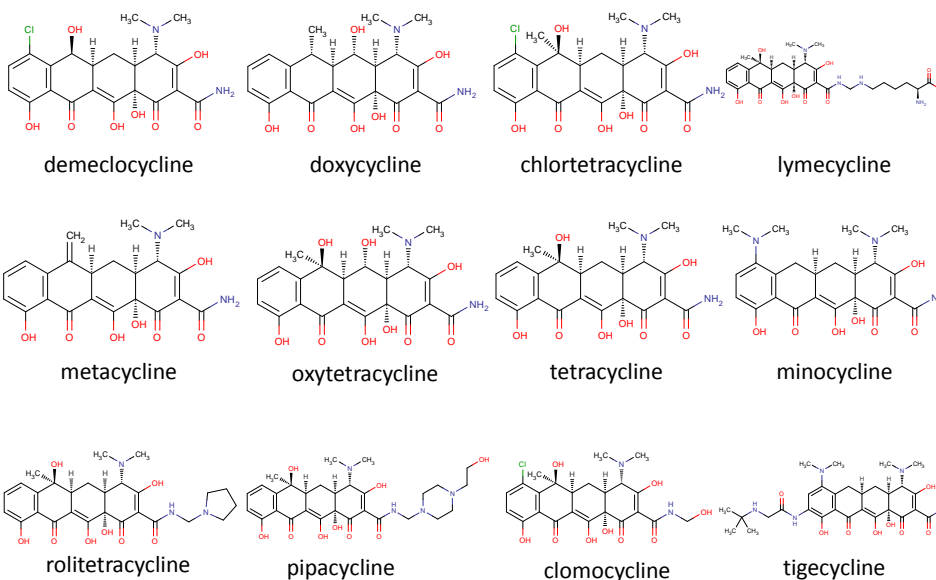
- New Public chemistry patent resource
- ‘Acquired’ SureChem product from Digital Science
 - Automatically extracted chemical structures from full-text patent
 - ~15 million chemical structures
 - Updated daily
 - Plan to add molecular target, sequence, disease, animal model, cell-line indexing....

Antibacterial Drug Targets

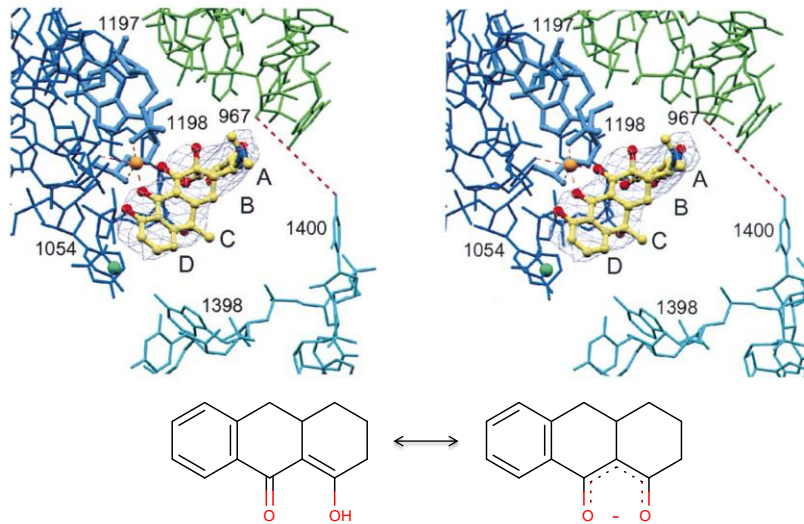
ATC Drug class	Target	Target type	Number of drugs
J01A Tetracyclines, J01G Aminoglycosides, J01XX Spectinomycin, J04AB Capreomycin	Ribosome 30S subunit	Riboprotein	24
J01B Amphenicols, J01F Macrolides, lincosamides, streptogramins, J01XX Linezolid	Ribosome 50S subunit	Riboprotein	22
J01XX Steroid antibiotics	Ribosome 70S ribosome-EF-G complex	Riboprotein	1
J01C Penicillins, J01D Cephalosporins, monobactams & carbapenems	Penicillin-binding proteins	Protein	85
J01C Bactams	Beta-lactamases	Protein	2
J01E Trimethoprim	DHFR	Protein	3
J01E Sulphonamides, J04AA Aminosallyclic acid, J04AB Dapsone, aldesulfone	Dihydropteroate synthase	Protein	23
J01M Quinolones	Topoisomerase II	Protein	27
J01XA Glycopeptides, J01XB Polymyxins, J01XD Imidazole derivatives, J01XE Nitrofurans derivatives, J01XX Xibornol, clofocetol, methenamine, mandelic acid, nitroxoline, daptomycin, bacitracin, J04AK Morinamide, delamanid, J04BA Clotrimazole	-	-	22
J01XX Fosfomycin	UDP-N-acetylglucosamine enolpyruvyl transferase	Protein	1
J04AB Cycloserine, J04AK Terizidone	Alanine racemase + D-Ala-D-Ala ligase	Protein	2
J04AB Rifampicin derivatives	DNA-dependent RNA polymerase	Protein	4
J04AC Isoniazid, J04AD Thiocarbamide derivatives	Enoyl-acyl carrier protein reductase	Protein	4
J04AK Ethambutol	Arabinosyl transferase	Protein	1
J04AK Pyrazinamide	Fatty Acid Synthase I	Protein	1
J04AK Bedaquiline	ATP Synthase	Protein	1

n.b. includes all antibacterial active ingredients with assigned ATC code

Approved Tetracycline Structures



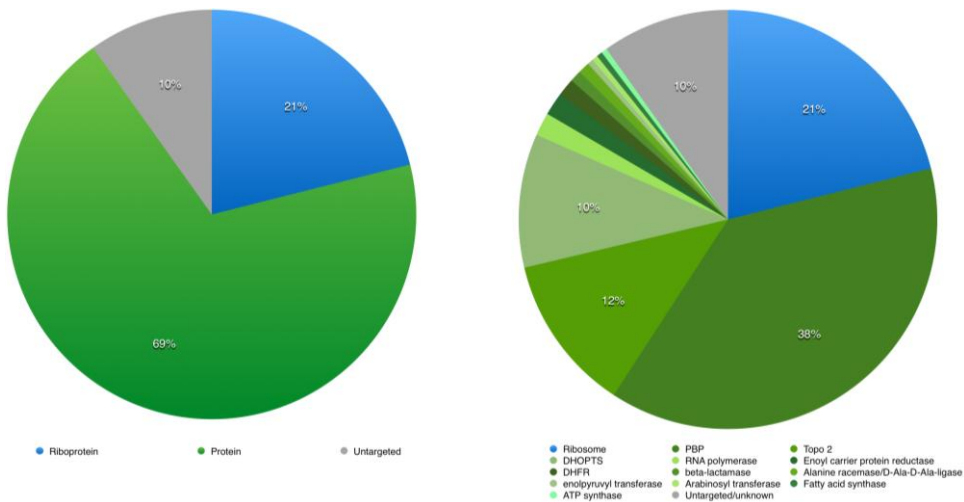
Tetracycline Binds 30S Ribosomal Subunit



Brodersen *et al. Cell*, **103** 1143–1154 (2000)

Antibacterial Drug Targets (J01 & J04)

N=223 drugs, 13 molecular targets – March 2014 ATC list

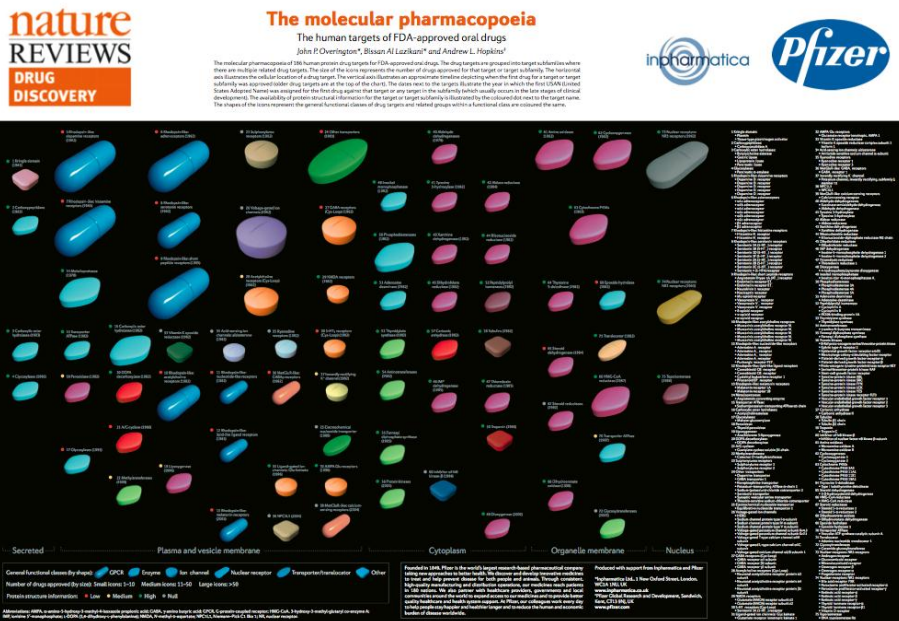


Santos & Overington *unpublished*

Audience Question

- What percentage of the human genome is a drug target?
- 53%
- 35%
- 8%
- 1%

Only ~1% of Genome is a Drug Target

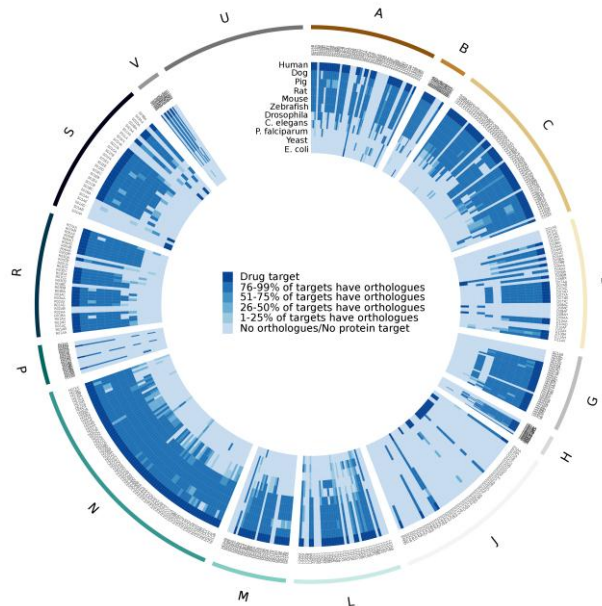


Drug Targets and Drugs

Drug target Class	Targets			Drugs		
	Total targets	Small-molecule drug targets	Biotherapeutic drug target	Total drugs	Small molecules	Biotherapeutics
Human Protein	315	243	86	1133	951	182
Pathogen Protein	52	49	4	205	200	5
Other human biomolecules	15	3	13	75	50	25
Other pathogen biomolecules	8	7	2	102	99	3

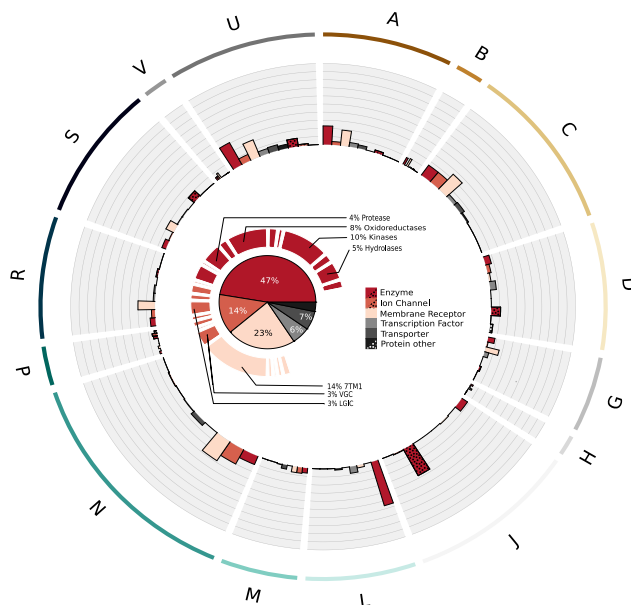
Santos *et al*, unpublished

Drug Targets Present in Model Organisms



Santos *et al*, unpublished

Drug Target Classes and Therapeutic Areas



Santos *et al*, unpublished

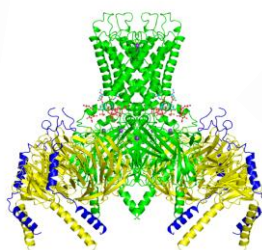
Privileged Target Families

Rhodopsin-like GPCR
PDBe: 3sn6



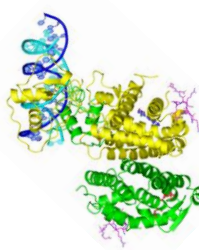
22% of drug targets
33% of small mol drugs

Ion channels
PDBe: 4kfm



12% of drug targets
18% of small mol drugs

Nuclear receptors
PDBe: 3e00



6% of drug targets
17% of small mol drugs

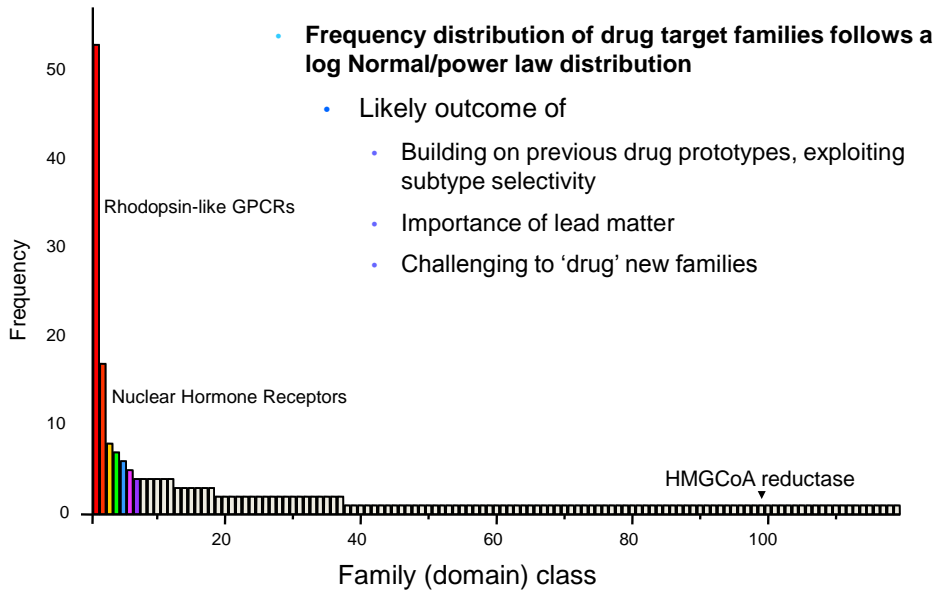
Protein kinases
PDBe: 4foc



13% of drug targets
2.4% of small mol drugs

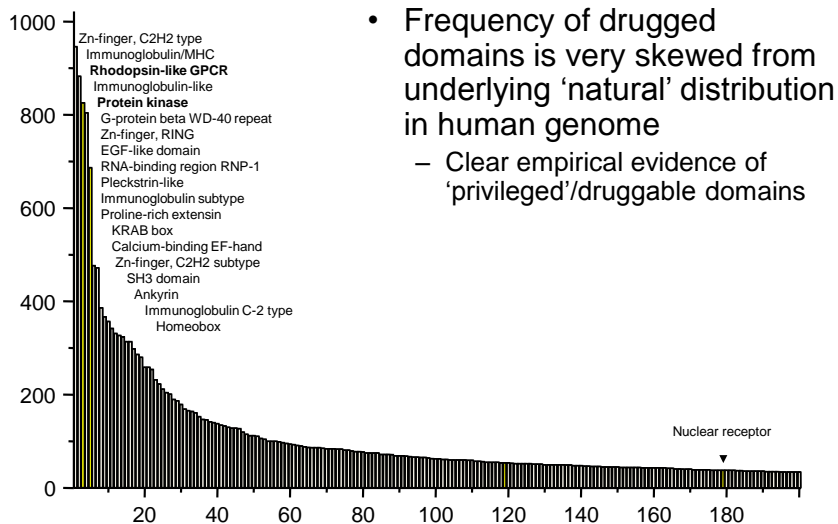
Over 53% of all targets and 70% of drugs modulate these four target classes

Molecular Targets of Current Drugs



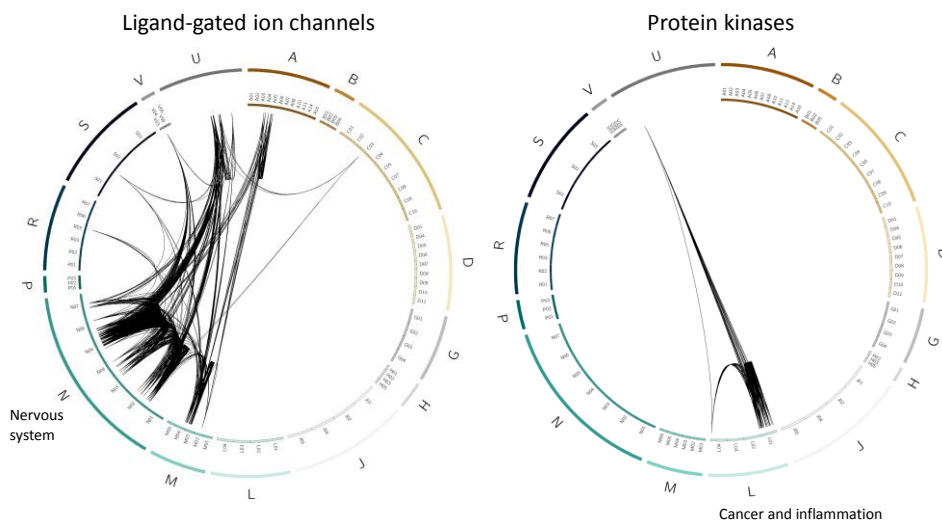
Overington, & Al-Lazikani *unpublished*

Domains within human genome



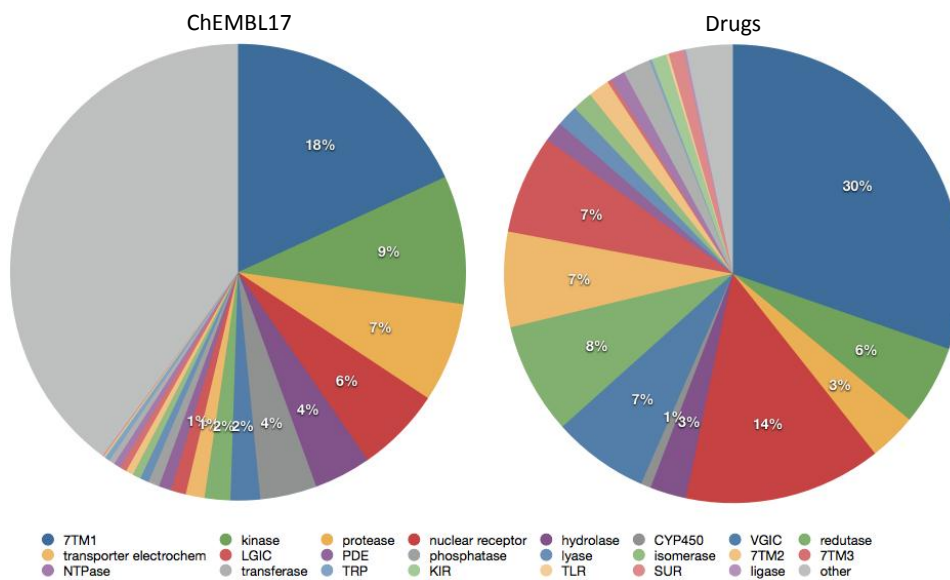
Overington, & Al-Lazikani *unpublished*

Footprint of Target Classes Across Disease



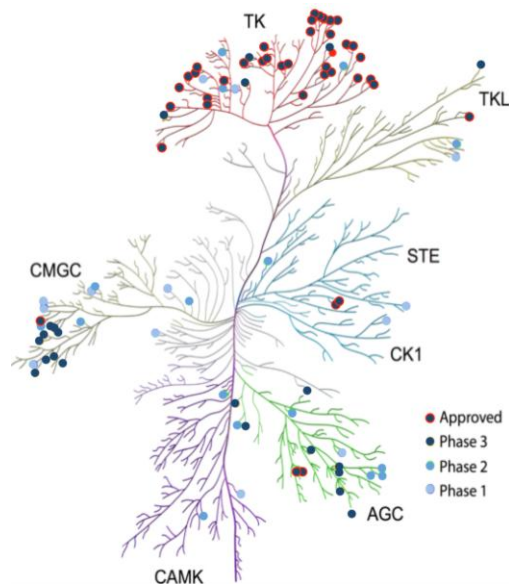
Santos *et al*, unpublished

Privileged Target Families



Santos, unpublished

Clinical Kinome



Overington, Al-Lazikani & Wennerberg, *unpublished*

Clinical Kinome

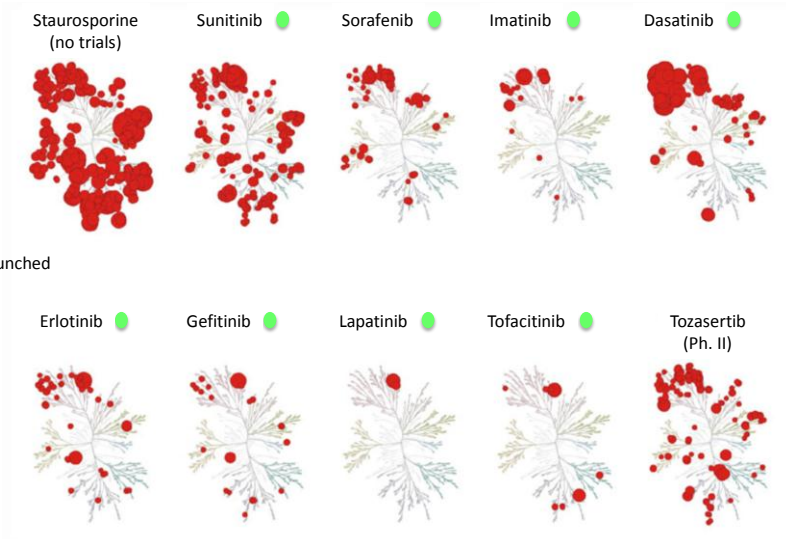
- 399 Clinical stage human kinase inhibitors
 - 29 Approved small molecule kinase inhibitors
 - 15 -tinib – tyrosine kinase inhibitors
 - 5 -rolimus – *mTor* inhibitors
 - 4 -rafenib – Raf inhibitors
 - 2 -anib – angiogenesis inhibitors
 - 1 -metinib – met inhibitor
 - 1 brutinib – Bruton tyrosine kinase inhibitors
 - 1 -dil – Rho kinase inhibitor (Japan only)
 - 38 Phase 3
 - 143 Phase 2
 - 189 Phase 1
 - Phase 1:2 ratio is atypical due to many kinase inhibitor trials being phase 1/2 oncology trials

Kinase Inhibitors in Clinical Development

Research Code	Research Code Alternative 1	Research Code Alternative 2	Research Code Alternative 3	Research Code Alternative 4	Research Code Alternative 5	USAN/INN	USAN Item	INN Year	Tradename US	Tradename EUR	Tradename JAP	ATCC	Wei ATCC	Htg Phase	Company	Class	Target Class
RG-1278						Afinib	irinib	2005	Irinia	Irinia		LQ1XK17	QLB1XK17	4 Phase	MTI (PDGFR) (VEGFR)	TK	multi (TK)
AMN-107	NVP-MM107					Nilotinib	nilotinib	2006	Tasigna	Tasigna		LQ1XK28	QLB1XK28	4 Novartis	ABL1 DDR1 KIT (PDGFR)	TK	multi (TK)
AP-2634						Pracinib	pracinib	2010	Ising	Ising		LQ1XK21	QLB1XK21	4 Amrad	ABL1 FLT3 (VEGFR) (PDGFR) TIE2	TK	multi (TK)
ACQ-1536	ZD-1536					Delitinib	delitinib	2010	Issa	Issa		LQ1XK36	QLB1XK36	4 AstraZeneca	EGFR ERBB2 ERBB4	TK	EGFR (TK)
BBW-2962						Afinib	irinib	2010	Glecap	Tovok		LQ1XK13	QLB1XK13	4 Boehringer Ingelheim	EGFR ERBB2	TK	EGFR (TK)
BMS-34625						Dasatinib	dasatinib	2005	Seyrel	Byyar		LQ1XK06	QLB1XK06	4 Bristol-Myers Squibb	ABL1 SRC TEC LYN LCK YES KIT EphA2 PDGFR	multi	multi (TK)
BMS-907351	XL-184					Cabozantinib	cabozantinib	2011	Cometriq			LQ1X0	QLB1X0	4 Bristol-Myers Squibb	MET VEGFR2	multi	multi (TK)
CP-696952						Tivozanib	tivozanib	2010	Belcan			LQ1X081	QLB1X081	4 Pfizer	JAK2 JAK3	TK	JAK (TK)
DW-872016	DW-2016					Lacotinib	lacotinib	2003	Tyverb	Tyverb		LQ1XK07	QLB1XK07	4 GlaxoSmithKline	EGFR ERBB2	TK	EGFR (TK)
NO5-18434	INC-424					Navitoclax	navitoclax	2010	Jakavi	Jakavi		LQ1XK16	QLB1XK16	4 Roche	JAK1 JAK2	TK	JAK (TK)
OS-774	CP-58874	R-1415	NSC-718761	RG-1415	No-508231	Erdotinib	erlotinib	2001	Tarceva			LQ1XK03	QLB1XK03	4 AstraZeneca	EGFR ERBB2	TK	EGFR (TK)
PF-0241966						Crizotinib	crizotinib	2009	Kabivo			LQ1XK16	QLB1XK16	4 Pfizer	ALK MET RON	multi	multi (TK)
PF-05209763	SK-606					Brigatinib	brigatinib	2002	Soulat			LQ1XK24	QLB1XK24	4 Pfizer	ABL1 SRC	multi	multi (TK)
STI-871	NVP-ST871	CGP-67146				Imatinib	imatinib	2003	Gleevec	Gleevec		LQ1XK01	QLB1XK01	4 Novartis	ABL1 DDR1 KIT (PDGFR)	multi	multi (TK)
SU-11248						Sunitinib	sunitinib	2006	Sutent	Sutent		LQ1XK04	QLB1XK04	4 Pfizer	FLT3 KIT (PDGFR) (VEGFR) Multiple	TK	multi (TK)
ABT-578						Zoledentus	zoledentus	2009	Entyvio	Rescula		LQ1X04	QLB1X04	4 Abbott	FKBP-12/MTOR	MTOR	MTOR (TK)
AY-22819						Rebentin	rebentin	1988	Requinone	Cypher		LQ4AA18	QLB1AA18	4 Pfizer	FKBP-12/MTOR	MTOR	MTOR (TK)
CC-779						Tamoxifen	tamoxifen	2004	Torise	Torise		LQ1XK09	QLB1XK09	4 Pfizer	FKBP-12/MTOR	MTOR	MTOR (TK)
PK-506						Fulvestrant	fulvestrant	1996	Fulvest	Pharlap	Pharlap	D11AK01	QLB1AK02	4 AstraZeneca	FKBP-12/Calcineurin	Calcineurin	Calcineurin (TK)
RGD-001	NVP-RAD001					Everolimus	everolimus	2002	Zorvea	Zortvan	Merce V	LQ1XK16	QLB1XK16	4 Novartis	FKBP-12/MTOR	MTOR	MTOR (TK)
SZC-434-981						Phascatinib	phascatinib	2000	Eled			D11AK02	QLB1AK02	4 Galderma	FKBP-12/Calcineurin	Calcineurin	Calcineurin (TK)
TM-100	Bu-9	A-9				Balutinib	balutinib	2008				D11AK02	QLB1AK02	4 Bioprocess International	FKBP-12/MTOR	MTOR	MTOR (TK)
BAY-43-8006						Sorafenib	sorafenib	2007	Nesovir	Nesovir		LQ1XK05	QLB1XK05	4 Bayer Health Care	KIT (PDGFR) RAF1 VEGFR2 VEGFR3	TK	multi (TK)
BAY-73-4806						Rapafaninib	rapafaninib	2008	Shingo			LQ1XK21	QLB1XK21	4 Bayer Health Care	ABL BAF1 DDR2 EphA2 (PDGFR) KIT (PDGFR) PTK2	TK	multi (TK)
DK-118436						Delavertinib	delavertinib	2011	Tahira			LQ1XK23	QLB1XK23	4 GlaxoSmithKline	BRM	RAF	
RG-7204	PLX-4032	No-6185426				Vemurafenib	vemurafenib	2010	Zelboraf	Zelboraf		LQ1XK15	QLB1XK15	4 Roche	BRM MEK1 MEK2 RAF1	RAF	RAF (TK)
OSK-1120212	JPR-76207					Tamoxifen	tamoxifen	2011	Meklore			LQ1XK09	QLB1XK09	4 GlaxoSmithKline	MEK1 MEK2	MEK	MEK (TK)
V-2102	AT-477	HA-1077				Fasudil	fasudil	1997	Ising			D04AK02	QLB1AK02	4 Ashi-Kasei Pharma	PDGFR	PDGFR (TK)	
AZD-6474	ZD-6474					Vandetanib	vandetanib	2006	Zactima	Claretia		LQ1XK13	QLB1XK13	4 AstraZeneca	EGFR (EPH) ERBB2 RET TIE2 BRK (VEGFR)	TK	multi (TK)
DW-78034						Pazopanib	pazopanib	2005	Vorlent	Vorlent		LQ1XK11	QLB1XK11	4 GlaxoSmithKline	KIT (PDGFR) (VEGFR)	TK	multi (TK)
AB-1010						Masitinib	masitinib	2007	Maszet			LQ1XK22	QLB1XK22	3 AB Science	FGFR3 KIT	TK	multi (TK)
AND-197						Tasitinib	tasitinib	2010				LQ1XK02	QLB1XK02	3 AstraZeneca	ABL1 SRC	TK	multi (TK)
AZD-0530	AZ-10353906					Sancatinib	sancatinib	2009				LQ1XK02	QLB1XK02	3 AstraZeneca	ABL1 SRC	TK	multi (TK)
BPL-2009H						Isatinib	isatinib					LQ1XK02	QLB1XK02	3 Beta Pharma	EGFR	TK	EGFR (TK)
CCP-701	KT-455	SP-824	SPR-924	A-154475		Larotrectinib	larotrectinib	2004				LQ1XK02	QLB1XK02	3 Teva	FLT3 JAK2 NTRK1 (PKC) RET	TK	multi (TK)
CI-1033	PD-183035	SN-29606				Carvatinib	carvatinib	2002				LQ1XK02	QLB1XK02	3 Pfizer	EGFR ERBB2	TK	EGFR (TK)
E-7090	ER-203492					Lemostatib	lemostatib	2010				LQ1XK02	QLB1XK02	3 Eisai	(VEGFR)	TK	VEGFR (TK)
HO-372	WKP-179272	CCP-820				Neratinib	neratinib	2006				LQ1XK02	QLB1XK02	3 Pfizer	EGFR ERBB2	TK	EGFR (TK)
IV-0811						Radotinib	radotinib	2011				LQ1XK02	QLB1XK02	3 Jyung Pharm	ABL1	TK	ABL (TK)

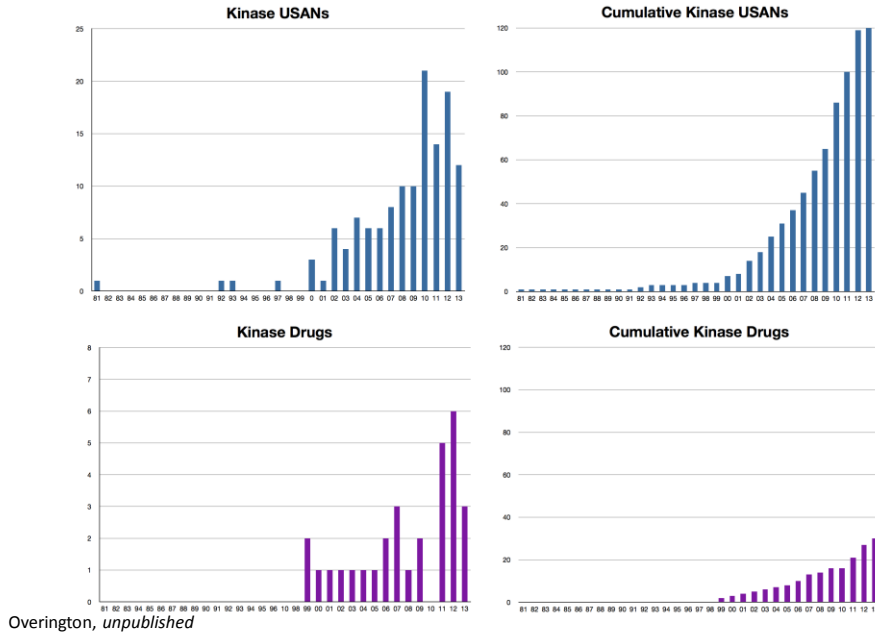
Overington, Bellis, Al-Lazikani & Wennerberg, unpublished

Kinase Inhibitor Polypharmacology



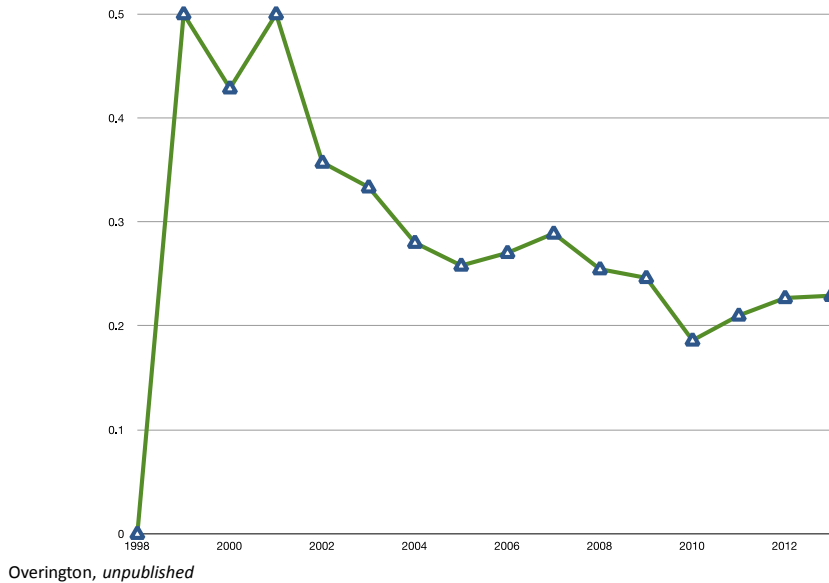
Adapted from Ghoreschi et al, Nature Immunology 10, 356 - 360 (2009)

Kinase Inhibitor Attrition

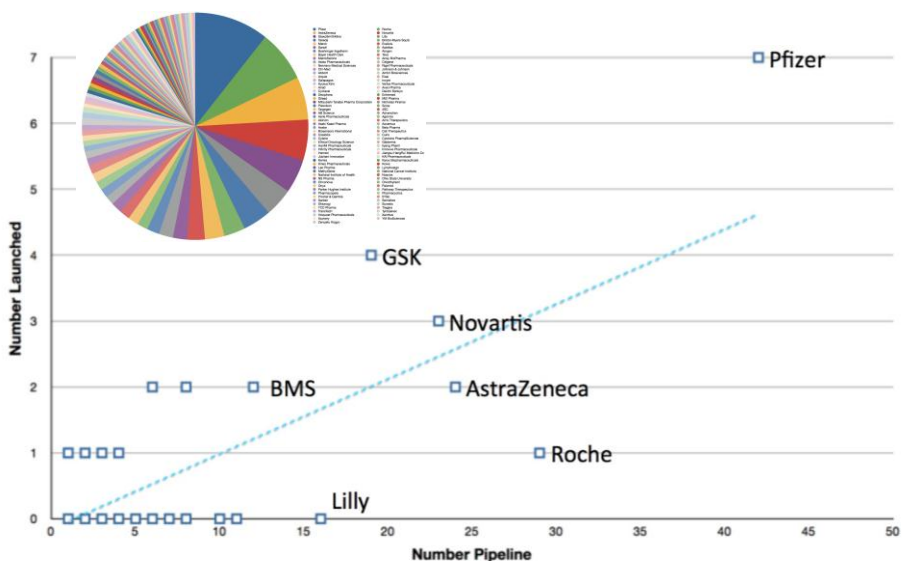


Kinase Inhibitor Attrition

USAN to approved fraction! – ~0.2 is long term mean for all drugs across all classes

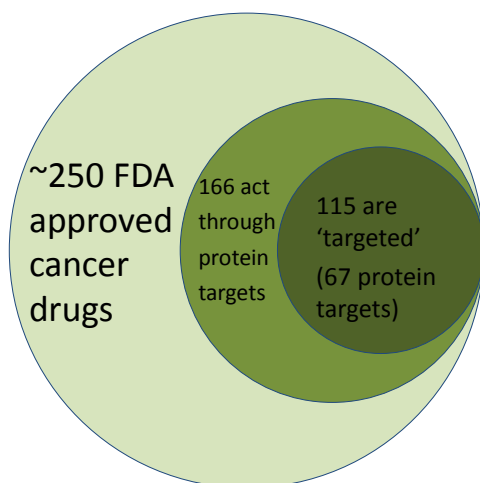


Kinase Inhibitor Productivity



Overington, unpublished

Cancer Drugs and Targets



Overington, Al-Lazikani, Hopkins, *Nat Rev Drug Discov.* 6 2006 5:993-6 (2008)

Updated in canSAR: Bulusu *et al*, *Nucleic Acids Res.* 42 D1040-7 (2014)



Cancer Genes

Science 29 March 2013:
Vol. 339 no. 6127 pp. 1546–1558
DOI: 10.1126/science.1235122



REVIEW

Cancer Genome Landscapes

Bert Vogelstein, Nickolas Papadopoulos, Victor E. Velculescu, Shihbin Zhou, Luis A. Diaz Jr., Kenneth W. Kinzler*



Mutational landscape and significance across 12 major cancer types

Cyrilac Kandoth, Michael D. McLellan, Fabio Vandin, Kai Ye, Beifang Niu, Charles Lu, Mingchao Xie, Qunyan Zhang, Joshua F. McMichael, Matthew A. Wyczalkowski, Mark D. M. Leiserson, Christopher A. Miller, John S. Welch, Matthew J. Walter, Michael C. Wendl, Timothy J. Ley, Richard K. Wilson, Benjamin J. Raphael & Li Ding

Affiliations | Contributions | Corresponding author

Nature 502, 333–339 (17 October 2013) | doi:10.1038/nature12634

Review



Nature Reviews Cancer 4, 177–183 (March 2004) | doi:10.1038/nrc1299

A census of human cancer genes

P. Andrew Futreal, Lachlan Coin, Mhairi Marshall, Thomas Down, Timothy Hubbard, Richard Wooster, Nazneen Rahman & Michael R. Stratton



Discovery and saturation analysis of cancer genes across 21 tumour types

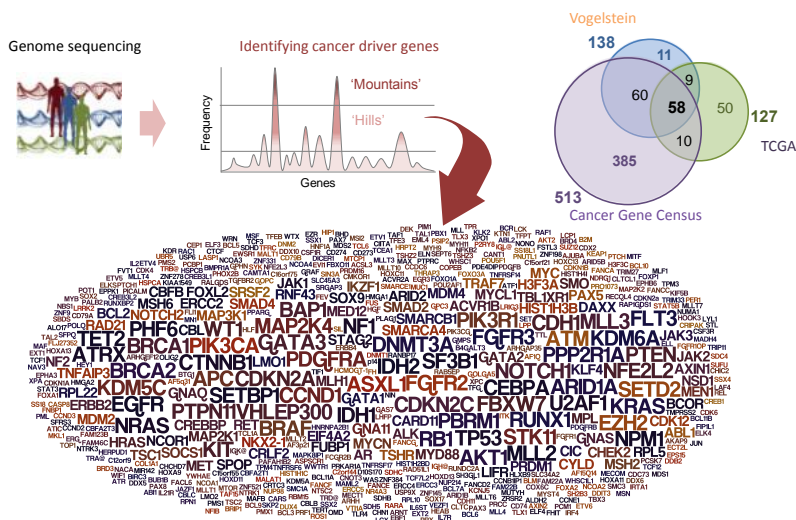
Michael S. Lawrence, Petar Stojanov, Craig H. Mermel, James T. Robinson, Levi A. Garraway, Todd R. Golub, Matthew Meyerson, Stacey B. Gabriel, Eric S. Lander & Gad Getz

Affiliations | Contributions | Corresponding authors

Nature 505, 495–501 (23 January 2014) | doi:10.1038/nature12912



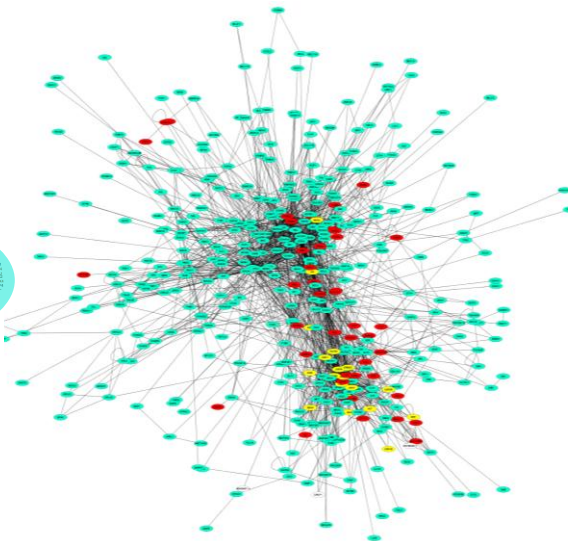
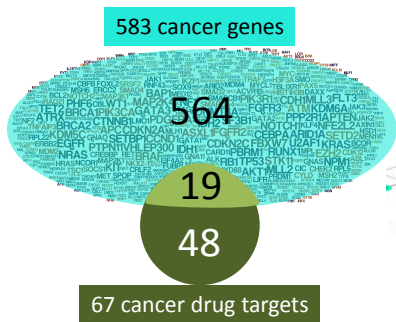
Cancer Genomics and Targets



Workman & Al-Lazikani, Nat. Rev. Drug. Discovery Nov 2013



Cancer Targets

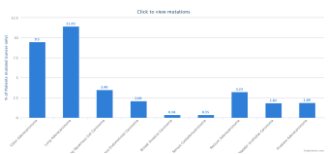
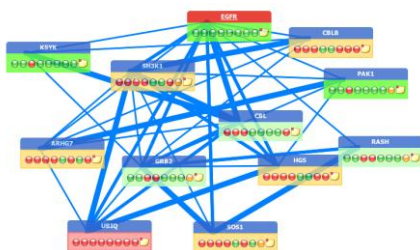


Al-Lazikani et al, unpublished

Genomic Data Integration

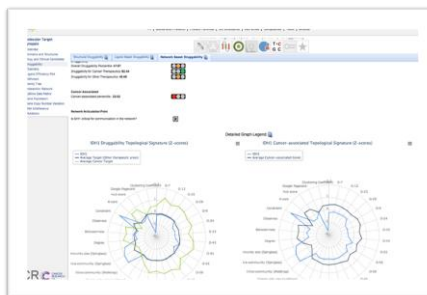
<http://cansar.icr.ac.uk>

Drug annotated target networks

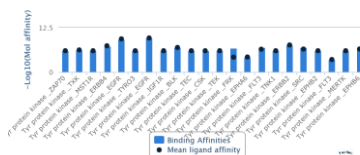


Mutation profiles

Network environment profiles



Protein Affinity Profile (395 molecular targets)



Drug activities



Bulusu et al, *Nucleic Acids Res.* 42 Jan;42:D1040-7 (2014)

Audience Question

What will the future of drug targets be focused on?

- GPCRs
- Nuclear Receptors
- Ion Channels
- Enzymes
- Non-Enzymes

Centre for Therapeutic Target Validation

- Collaboration to pinpoint processes in the human body that impact on disease.
- Public-private initiative:
 - **GSK**: expertise in disease biology and translational medicine
 - **EMBL-EBI**: expertise in life science data integration and analysis
 - Wellcome Trust Sanger Institute: expertise in the role of genetics in disease



Acknowledgements

ChEMBL Database

Anne Hersey
Anna Gaulton
Mark Davies
Michal Nowotka
George Papadatos
Jon Chambers
Louisa Bellis
Rita Santos
Gerard Van Westen
Ruth Akhtar
Francis Atkinson
Patricia Bento
Ramesh Donadi
John Paul Overington

Institute of Cancer Research

Bissan Al-Lazikani
Paul Workman

FIMM, Helsinki

Krister Wennerberg

University of Dundee

Andrew Hopkins

The ChEMBL-og
The Organization of Drug Discovery Data

Resources: ChEMBL | SureChEMBL | ChEMBL-NTD | ChEMBL-Malaria | SARfari | GPCR Kinase ADME | UniChem | DrugEfficacy

Monday, 13 January 2014

ADME SARfari: A tool for predicting and comparing cross-species ADME targets

ADME studies are focused on understanding the disposition of a compound within an organism and the results of such studies play a critical role in the drug development process. ADME studies (more commonly referred to as pharmacokinetic or PK studies) are focused on 4 main areas: Absorption, Distribution, Metabolism and Excretion. More information on the PK measurement types can be found here.

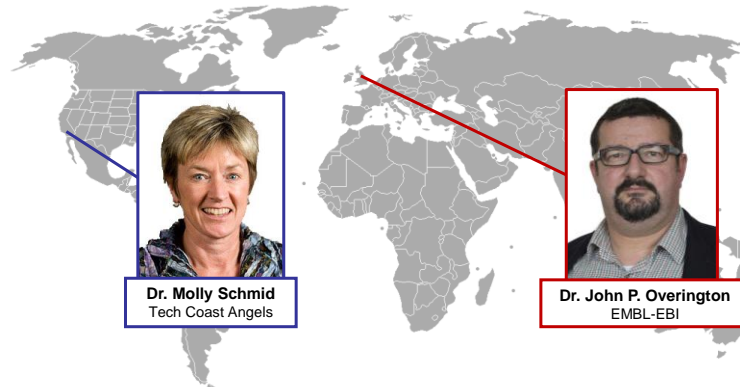
Comparisons of PK data across species is a potential problem drug researchers need to deal with, as model organism studies are the primary source of such data. For example, in an animal model study, which may be carried out on a compound as it passes through the drug development pipeline, is it meaningful to compare clearance or bioavailability data from a mouse or rat to human? Clearly there are many differences (physique, metabolic, genetic,...) which make answering these types of questions difficult. Building tools which guide researchers to potential answers or provide a better understanding of the inter-species differences are of great value - leading us nicely to the focus of this blog post.

<http://chembl.blogspot.com>

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Chris Lipinski, Melior Discovery

Dr. Tudor Oprea, UNM School of Medicine, DTU Center for
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Elizabeth Hamelin, Centers for Disease Control and
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Lucas Zarwell, Chief Toxicologist, District of Columbia



Thursday, April 10, 2014

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Darcy J. Gentleman, Ph.D, Science communicator, ACS
Office of Public Affairs

Kathryn Verona, ACS Office of Public Affairs

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Dr. Molly Schmid
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